

23. The composition of claim 22, wherein the hPTH (1-84) is nearly homogeneous.

*Sub D7* 24. A composition comprising recombinant human parathyroid hormone (hPTH) (1-84), wherein the hPTH is made by a process comprising the steps of:

- (a) providing a microorganism comprising:
  - (1) a leader sequence corresponding to the DNA sequence encoding *Saccharomyces* mating factor  $\alpha 1$  lacking the yeast STE13 recognition; and
  - (2) a DNA sequence encoding hPTH, wherein the leader sequence and the hPTH sequence are operably linked;
- (b) culturing said microorganism to allow expression of said DNA sequence encoding hPTH, thereby producing hPTH (1-84); and
- (c) purifying the resultant hPTH (1-84) protein.

*Sub D8* 25. The composition of claim 24, wherein the microorganism is selected from the group consisting of *Escherichia coli* and yeast.

*Sub D8* 26. The composition of claim 24, wherein the hPTH protein has a purity of greater than 90%.

27. A composition comprising recombinant human parathyroid hormone (hPTH) (1-84), wherein the hPTH is made by a process comprising the steps of:

- (a) providing a microorganism comprising:
  - (1) the first nineteen amino acids of the DNA sequence encoding *Saccharomyces* mating factor  $\alpha 1$  as a leader sequence; and
  - (2) a DNA sequence encoding hPTH, wherein the leader sequence and the hPTH sequence are operably linked;
- (b) culturing said microorganism to allow expression of said DNA sequence encoding hPTH, thereby producing hPTH (1-84); and

(c) purifying the resultant hPTH (1-84) protein.

28. The composition of claim 27, wherein the microorganism is selected from the group consisting of *Escherichia coli* and yeast.

*Sub D9* 29. The composition of claim 27, wherein the protein has a purity of greater than 90%.

30. A composition comprising recombinant human parathyroid hormone (hPTH) (1-84), wherein the hPTH is made by a process comprising the steps of:

(a) providing a microorganism comprising:

(1) a leader sequence; and

(2) a DNA sequence encoding a derivative of hPTH, wherein the cleavage site after the pair of basic amino acids at positions 25 and 26 of the derivative hPTH gene has been modified such that the hormone is excluded as a substrate for yscF protease, wherein the leader sequence and the hPTH sequence are operably linked;

(b) culturing said microorganism to allow expression of said DNA sequence encoding hPTH, thereby producing hPTH (1-84); and

(c) purifying the resultant hPTH (1-84) protein.

31. The composition of claim 30, wherein amino acid 26 of the human hPTH gene is modified from lysine to glutamine.

32. The composition of claim 30, wherein the leader sequence is the DNA sequence encoding *Saccharomyces* mating factor  $\alpha 1$ .

33. The composition of claim 30, wherein the protein has a purity of greater than 90%.

34. A composition comprising recombinant parathyroid hormone (hPTH) (1-84), wherein the hPTH is made by a process comprising the steps of:

- See D1*
- (a) providing a microorganism comprising:
    - (1) a leader sequence; and
    - (2) a DNA sequence encoding hPTH comprising an optimized consensus signal sequence having the following:
      - (i) a positively charged amino-terminal;
      - (ii) a hydrophobic core region; and
      - (iii) a polar COOH-terminal region,wherein the leader sequence and the hPTH sequence are operably linked;
  - (b) culturing said microorganism to allow expression of said DNA sequence encoding hPTH, thereby producing hPTH (1-84); and
  - (c) purifying the resultant hPTH (1-84) protein.

35. The composition of claim 34, wherein the signal sequence is encoded by an amino acid sequence selected from the group consisting of: (1) Met-Lys-Ala-Lys-Leu-Leu-Val-Leu-Leu-Thr-Ala-Phe-Val-Ala-Thr-Asp-Ala; (2) Met-Arg-Ser-Leu-Leu-Ile-Leu-Val-Leu-Cys-Phe-Leu-Pro-Leu-Ala-Ala-Leu-Gly; and (3) Met-Arg-Phe-Pro-Ser-Ile-Phe-Thr-Ala-Val-Leu-Phe-Ala-Ala-Ser-Ser-Ala-Leu-Ala.

*See D11*

36. A composition comprising recombinant parathyroid hormone (hPTH) (1-84), wherein the hPTH is made by a process comprising the steps of:

- (a) providing a microorganism comprising:
  - (1) a leader sequence; and
  - (2) a DNA sequence encoding hPTH comprising a functional signal sequence encoded by an amino-terminal amino acid sequence, the expression product of which can direct secretion in yeast, wherein the leader sequence and the hPTH sequence are operably linked;
- (b) culturing said microorganism to allow expression of said DNA sequence encoding hPTH, thereby producing hPTH (1-84); and